MOLECULAR EXPLANATIONS FOR TOXICITY OF OXYGEN

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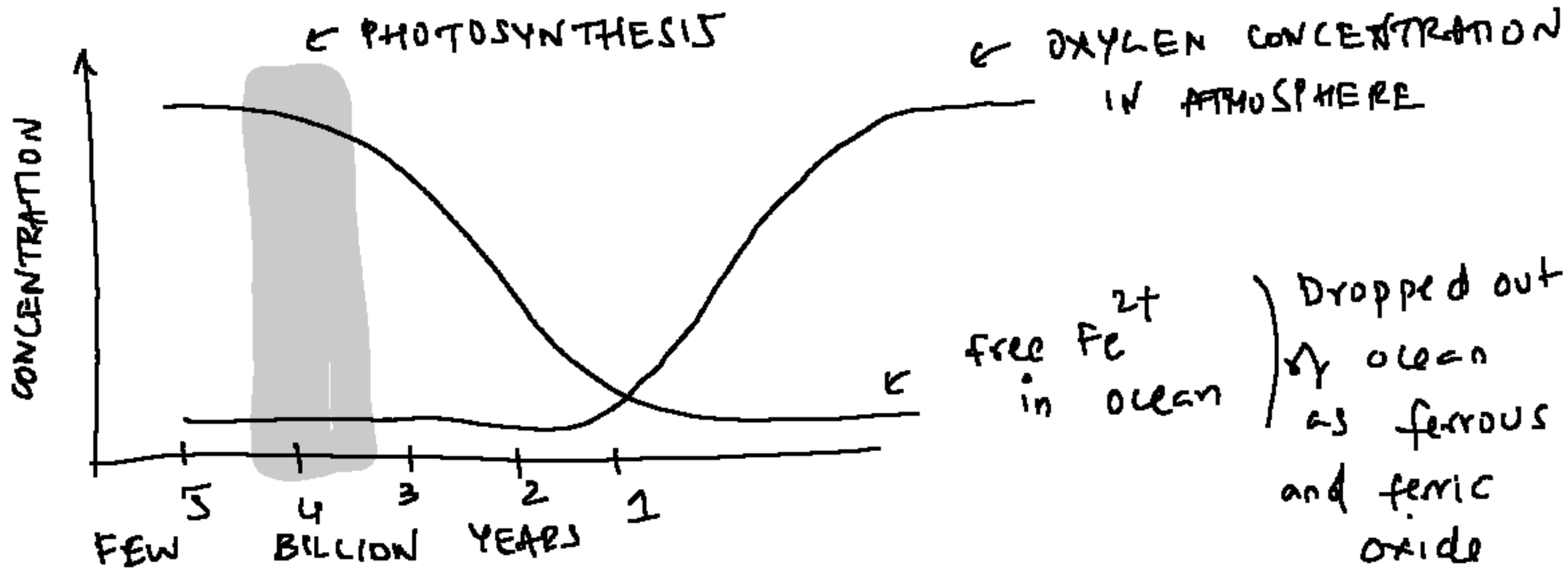
(1) WHY IS OXYGEN TOXIC?



REASON (SPECULATION ?):-

→ BIOCHEMISTRY OF LIFE EVOLVED IN THE ABSENCE OF OXYGEN & PRESENCE OF FREE Fe^{2+}.

→ ENZYMES USE IRON AS COFACTOR DUE TO ITS ABUNDANCE DURING EARLY STAGES OF EVOLUTION

→ OXYGEN TOXICITY IS A CONFLICT BETWEEN OLD Fe^{2+} BASED SYSTEMS AND OXYGEN BASED RESPIRATION

(2) HOW IS OXYGEN TOXIC? (MECHANISMS)

(a) MAKES ENZYMES INEFFECTIVE

Flavoenzymes (contains Fe^{2+} cofactor) donates electrons in biochemical pathways

O_2 diffuses in, absorbs electrons, becomes H_2O_2 (hydrogen peroxide)

H_2O_2 can diffuse into open enzymes and donate electrons to Fe^{2+} or other metals modifying enzyme structure & making it ineffective

→ Fe^{2+} IS EASILY OXIDISED BY OXYGEN, CAUSING OXYGEN TO MESS WITH ENZYME FUNCTION.

→ CONSEQUENCE OF BIOCHEMISTRY. H_2O_2 PRODUCTION IN CELL IS INEVITABLE

(b) DNA DAMAGE

H_2O_2 diffuses into nucleus, reacts with Fe^{2+} near DNA (Fe^{2+} is floating in cell, abundantly) producing free radicals (O^-, O^{2-}, OH^- etc) that react with DNA

→ DNA DAMAGE PREVENTION MECHANISMS REMOVE H_2O_2 IN NUCLEUS AND SEQUESTER FREE Fe^{2+} TO REDUCE FREE RADICAL PRODUCTION.

C3) CAN OXYGEN TOXICITY BE USED TO DEVELOP ANTI-BACTERIAL OR ANTI-TUMOR DRUGS?

JUGLONE - FROM WALNUTS

↳ CAUSES OXIDATIVE STRESS THAT INHIBITS PLANT GROWTH IN VICINITY OF THE TREE

↳ CAUSES H_2O_2 production in cells by diffusing inside cells

(CH_4O_2 cannot easily diffuse into cells)

↳ HARD TO KILL CELLS DUE TO OXIDATIVE STRESS PREVENTION MECHANISMS

(QUICK RESISTANCE)

STREPTONIGRIN

↳ CAUSES DNA DAMAGE BY BINDING Fe^{2+} CLOSE TO DNA AND PRODUCING FREE RADICALS DIRECTLY.

↳ DOES NOT CAUSE DNA DAMAGE THROUGH H_2O_2 PRODUCTION, SO CIRCUMVENTS DAMAGE PROTECTION MECHANISMS.